The Evidence Base for Women




Dr. Busisiwe Msimanga-Radebe
WHO South Africa country office

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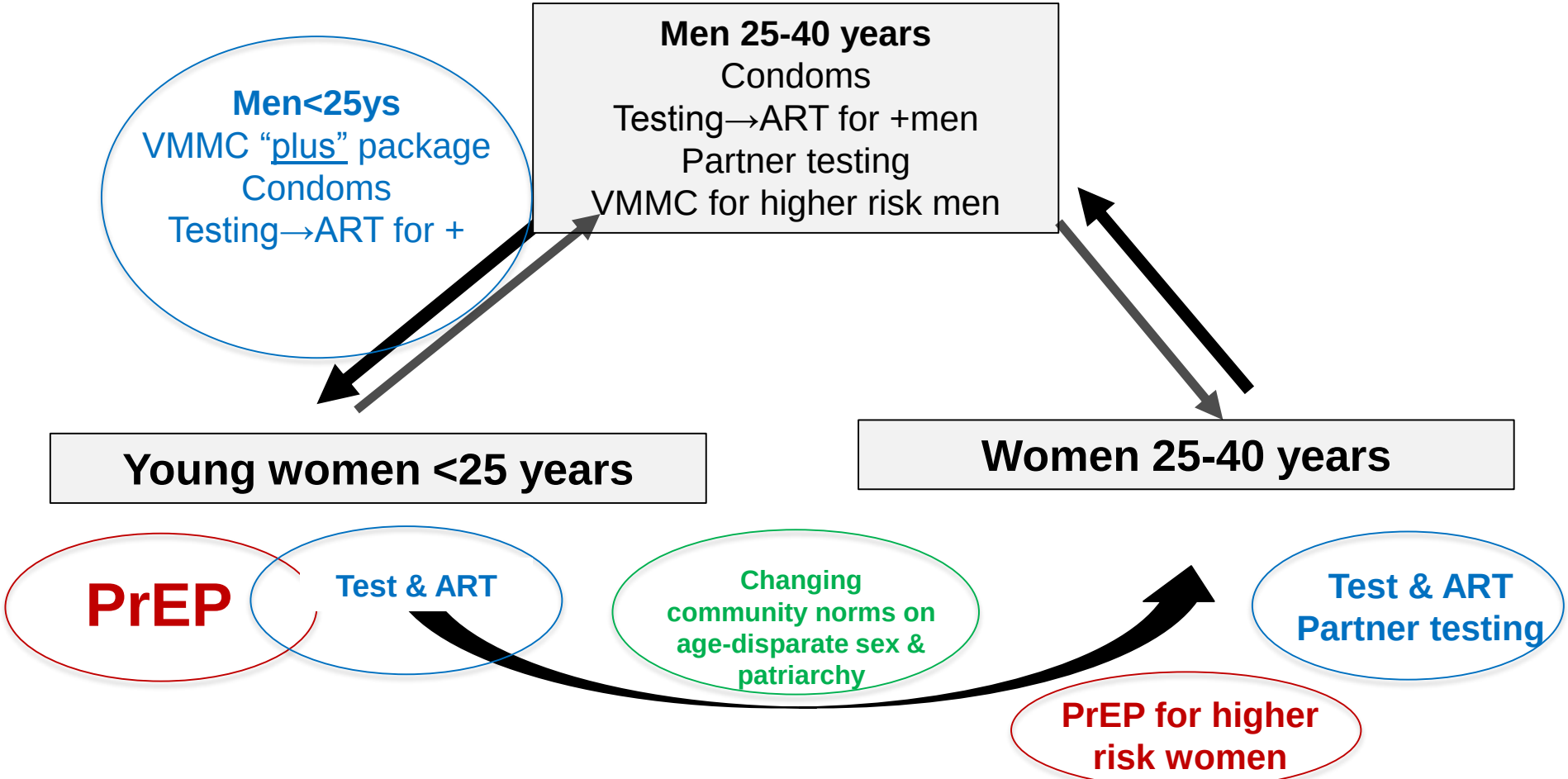
Abidjan, Cote d'Ivoire

World Health Organization

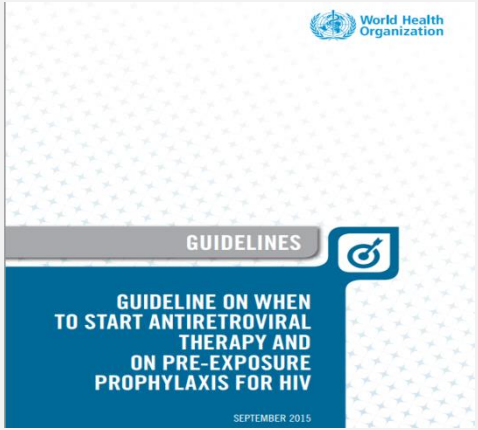
Combination prevention to break the cycle of HIV transmission



WHO recommendation for PrEP

Oral PrEP (containing TDF) should be offered as an additional prevention choice for people at *substantial risk* of HIV infection as part of combination prevention approaches

- **Enabling recommendation**
- **Not population specific**
  - For people ***at substantial HIV risk*** (provisionally defined as HIV incidence > 3 per 100 person–years in the absence of PrEP)
- Offer as an ***additional prevention choice***
- Provide PrEP within ***combination prevention***
  - Condoms and lube
  - Harm reduction
  - HIV testing and links to ART
- Provide PrEP with ***comprehensive support***
  - Adherence counselling
  - Legal and social support
  - Mental health and emotional support
  - Contraception and reproductive health services



WHO PrEP Implementation Tool (2017)

http://who.int/hiv/pub/prep/prep-implementation-tool

- Modular
- Different audiences
- Different setting
- Different populations
- Suggestions not recommendations
- Much uncertainly
- Learn as implement
- Frequent updating anticipated

Recurrent concerns expressed by MoH

Cost	Why should we prioritize PrEP when treatment is our immediate priority?
Where, Who	Where do we start? Which populations ? Where to offer services?
Safety	'Toxic drugs' for people without HIV
Drug resistance	People taking PrEP, esp. with poor adherence: Will this result in lots of drug resistance ?
Behavioral disinhibition	Offering PrEP will mean people stop using condoms, have more sexual partners, more STIs
Pregnancy and hormonal contraception	PrEP isn't safe during pregnancy and should be stopped when women become pregnant What about drug interactions?
Adherence	Lots of the trials had poor results with poor adherence
< 18 years	Many concerns esp. for adolescent girls e.g. safety, feasibility, adherence, perception of risk, parental consent

PrEP and women – key issues

- **Mixed "results" from trials**

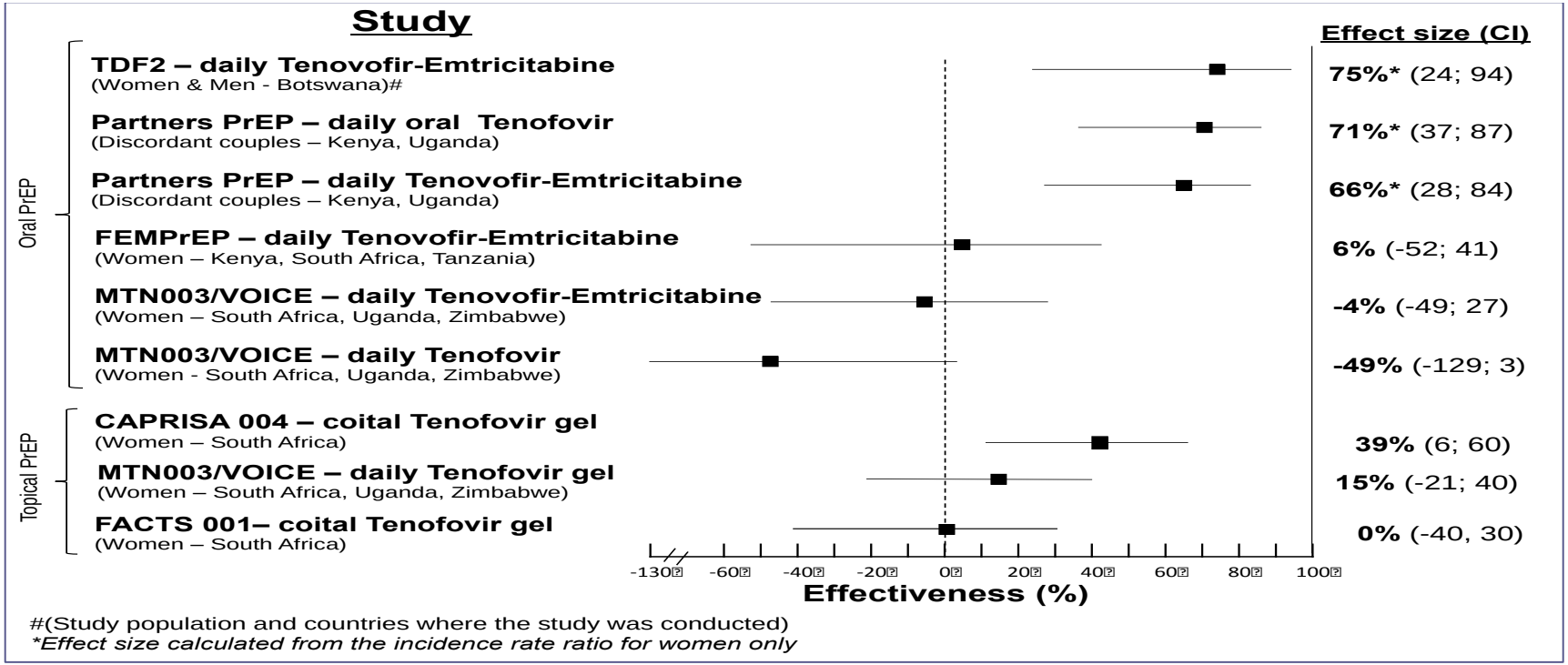
- **Very little real world experience for women**
  - Even less for adolescent girls
  - More (and increasing experience from sex worker projects)

- **How to prioritize implementation**
  - All women – overwhelming and unfeasible
  - Women at highest risk – often have multiple vulnerabilities
  - Women who want PrEP – may have self-identified high risk and more motivated to adhere
  - Balance between offering PrEP to women at substantial risk vs stigmatizing PrEP as something for 'risky women'

- **Adherence is key**
  - Good adherence in SDC trials and OLE
  - Poor adherence – commonly observed in other trials, esp younger women
  - Understanding poor adherence
  - Supporting better adherence

- **Where to offer PrEP for women**
  - ANC clinics, Family planning, STI services, Primary health care, ART clinics

Effectiveness of TDF and TDF/FTC antiretroviral pills & gels in women



#(Study population and countries where the study was conducted)

**Effect size calculated from the incidence rate ratio for women only*

Varying outcomes from PrEP trials - attributed to adherence

PrEP ‘less forgiving’ for women compare to MSM

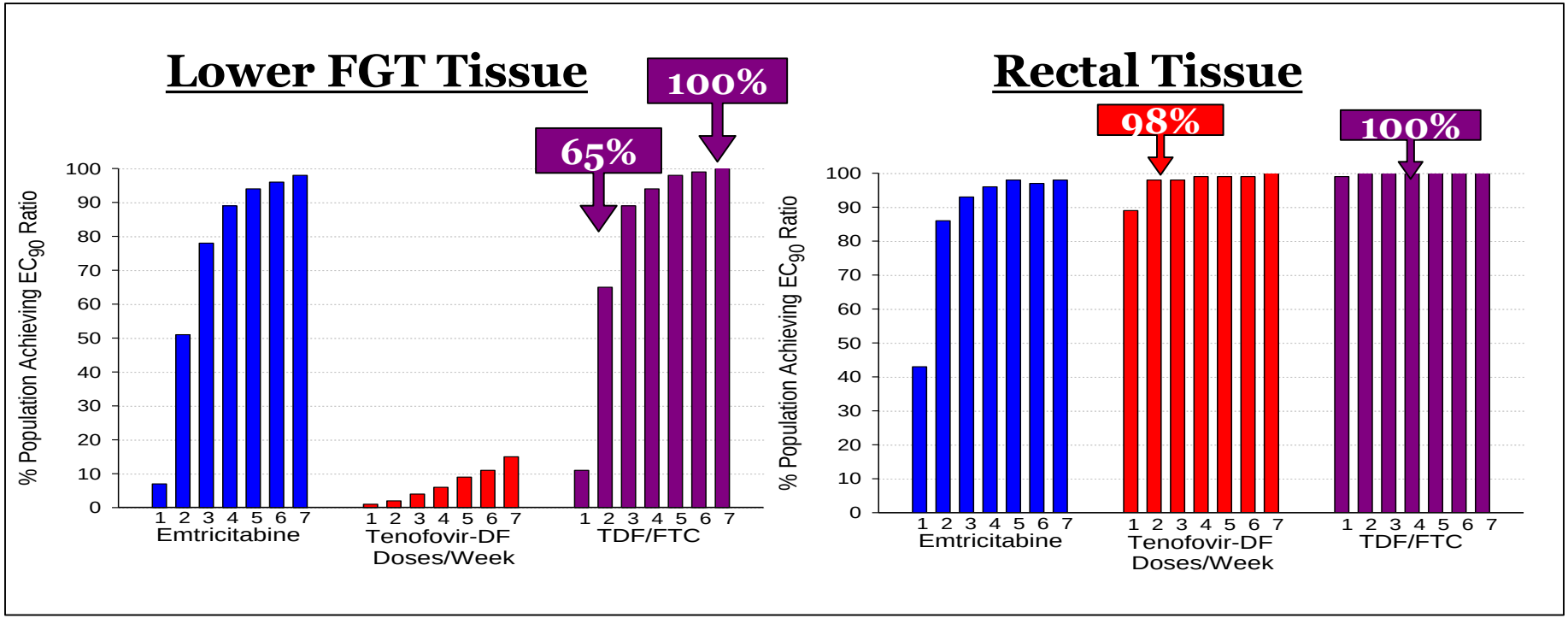
Message: PrEP reaches effective steady sate levels effectiveness after approximately 7 doses.

- *Protection likely to be adequate after **7 daily doses for women** having **vaginal sex** (PK studies from vaginal tissue)*
- *Protected likely to be adequate after **7 daily does for men** having **penile-vaginal sex** (very limited PK data from penile tissue) men*
- *Protected likely to be adequate after <**daily doses** for **anal sex** (PK studies from rectal tissue)*

Event driven PrEP (eg Ipergay regime) shown from RCT to be effective for MSM – no studies for women – but unlikely to give adequate protection

Grant RM et al (2014), Molina JM et al (2015), Seifert SM et al (2015), Cottrell M et al (2016), and Grant RM et al (2015)

“Time to effectiveness” in lower female genital tract (FGT) vs rectal tissue

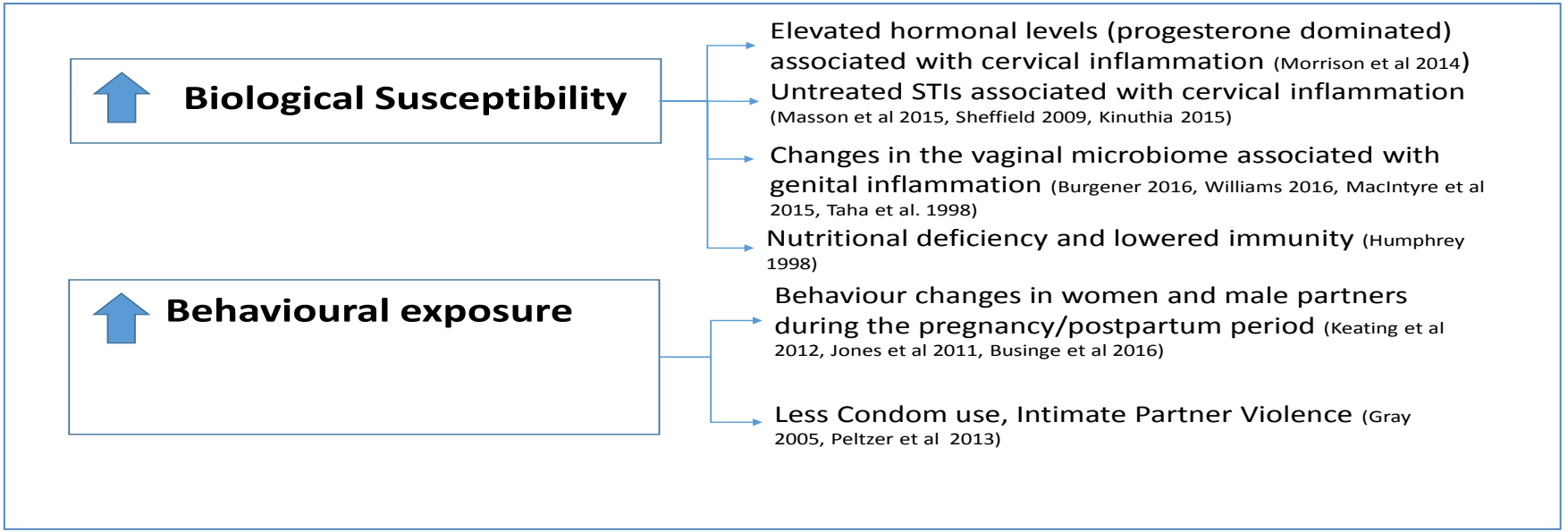


Cottrell ML et al. *J Infect Dis*. 2016 Jul 1;214(1):55-64.

Multiple ongoing PrEP studies in young African women, including

Study, funder, PIs	N & locations	What it will teach us
HPTN 082/HERS (NIH) Pis: Celum, Delaney-Moretlwe	400 women ages 16-25 (**Harare, Joburg, & Cape Town**)	• Uptake; • Adherence with CBT counseling & 2 way SMS; • Effect of drug level feedback on adherence
3Ps (NIH & BMGF) Pis: Bekker, Celum	200 women ages 16-25 (**Cape Town**)	• Uptake with creative marketing campaign; • Effect of incentives conditioned on drug levels on adherence
POWER (USAID) Pis: Baeten, Celum	3000 women ages 16-25 (**Cape Town, Joburg, Kisumu**)	• Emphasis on scalable delivery models • Use of a decision support tool
MTN 034 /REACH Pis: Nair, Ngure, Celum	300 women ages 16-21 (**Cape Town, Durban, Joburg, Harare, Kisumu**)	• Cross-over study to evaluate safety of oral TDF/FTC PrEP & dapivirine ring • Adherence • Preference of oral PrEP vs dapivirine ring

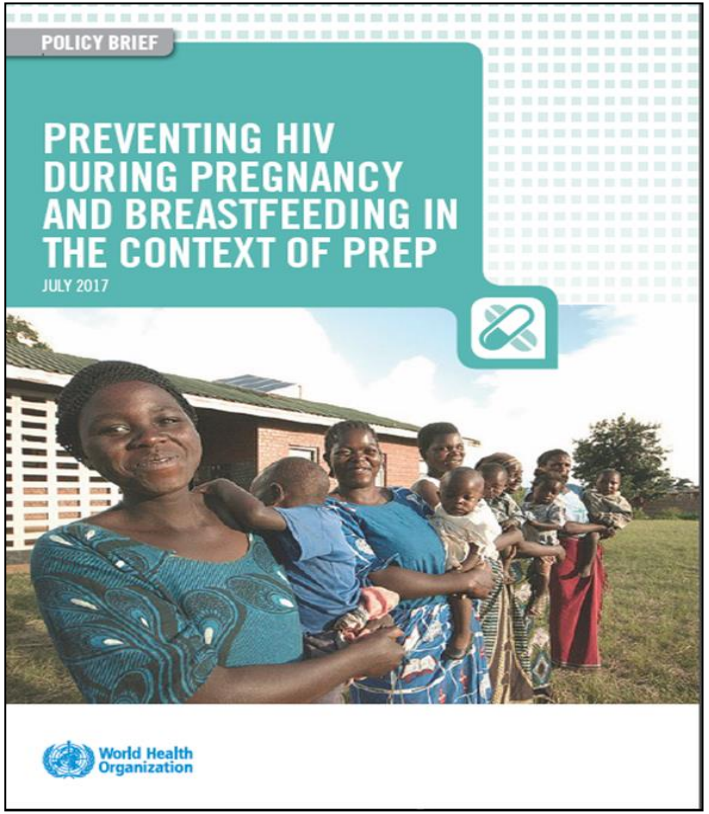
PrEP in Pregnancy and BF: The rationale



- In some countries, PrEP discontinued when women at substantial HIV risk become pregnant
- HIV acquired during pregnancy/BF can be transmitted to infant
- In high prevalence settings, women at substantial HIV risk ***wishing to conceive*** may include those whose partners have HIV but are not virally suppressed, or whose status is unknown

WHO Technical Brief:

Preventing HIV during pregnancy and breastfeeding in the context of PrEP



- Given the available safety data, there does not appear to be a safety-related rationale for discontinuing PrEP during pregnancy and breastfeeding for HIV-uninfected women receiving PrEP who become pregnant and remain at continuing risk of HIV acquisition.
- In such situations, the risk of HIV acquisition and accompanying increased risk of mother-to-child HIV transmission appears to far outweigh the potential risk of fetal and infant exposure to TDF used for PrEP.
- The final decision on whether to continue PrEP during pregnancy and breastfeeding should be made **by the pregnant woman** in consultation with her health care worker, balancing risks on HIV acquisition against potential harms
- **Additional surveillance** is important

IMPAACT 2009 (DAIDS ID 30020)

Feasibility, acceptability and safety of oral PrEP during pregnancy and breastfeeding in AGYW (16-24 years)

International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network

Observational cohort study of HIV-uninfected pregnant AGYW designed to

- characterize *adherence* over time among AGYW who initiate once daily PrEP during pregnancy & continue for 6 months following delivery
- compare pregnancy outcomes among women who take PrEP and women who decline PrEP during the AN period.
- Study sites in Zimbabwe, South Africa, Malawi, Uganda

IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

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